

WHAT IS CLAIMED IS:

1. A method of screening an agent for activity in modulating T lymphocyte function, the method comprising:

(1) contacting the agent with

(a) a cell expressing a HSV U_S3 polypeptide and one or more other HSV proteins; and/or

(b) a T lymphocyte;

(2) contacting the HSV U_S3-expressing cell with the T lymphocyte;

(3) contacting a second HSV U_S3-expressing cell with a second T lymphocyte, wherein the second HSV U_S3-expressing cell and the second T lymphocyte are not contacted with the agent;

(4) determining for each of the first and second T lymphocyte the level of a physiological change associated with T lymphocyte function; and

(5) comparing the relative levels of the physiological change determined for each of the first and second T lymphocytes to determine whether the agent modulates T lymphocyte function.

2. The method of claim 1, further comprising contacting the first and second T lymphocytes with a second agent that activates the T cell receptor (TcR-activating agent).

3. The method of claim 1, wherein the cell expressing the HSV U_S3 polypeptide and late HSV proteins is infected with herpes simplex virus (HSV).

4. The method of claim 3, wherein the HSV is HSV-1 or HSV-2.

5. The method of claim 1, wherein the cell expressing the HSV U_S3 polypeptide and HSV proteins is a recombinant cell.

6. The method of claim 1, wherein the HSV U_S3 polypeptide has an amino acid sequence that has 90% sequence identity with the sequence set forth in SEQ ID NO:1 or SEQ ID NO:2.

7. The method of claim 6, wherein the HSV U_S3 polypeptide has the amino acid sequence set forth in SEQ ID NO:1 or SEQ ID NO:2.

8. The method of claim 1, wherein the cell expressing the HSV U_S3 polypeptide is a fibroblast.

9. The method of claim 1, wherein the physiological change is production of a cytokine.

5 10. The method of claim 9, wherein the cytokine is selected from the group consisting of IFN- γ and TNF- α .

11. The method of claim 1, wherein the physiological change is exocytosis of lytic granules from the T lymphocyte.

10 12. The method of claim 1, wherein the physiological change is a change in the relative phosphorylation level of a cellular protein.

13. The method of claim 12, wherein the cellular protein is a cytotoxic T lymphocyte (CTL) protein.

14. The method of claim 13, wherein the CTL cellular protein is associated with the TcR or the TcR signaling cascade.

15 15. The method of claim 13, wherein the CTL cellular protein is heat shock protein 90 (HSP90) or a 50 kD protein.

16. The method of claim 15, wherein the phosphorylation of HSP90 and/or the 50 kD protein is increased.

20 17. The method of claim 15, wherein the phosphorylation of HSP90 and/or the 50 kD CTL protein is decreased.

18. The method of claim 2, wherein the TcR-activating agent is staphylococcal enterotoxin B (SEB).

19. The method of claim 2, wherein the TcR-activating agent is an anti-CD3 antibody.

25 20. The method of claim 19, wherein the anti-CD3 antibody is immobilized on a solid phase.

21. The method of claim 19, further comprising contacting the T lymphocyte with a target cell expressing Fcγ receptor.

22. The method of claim 21, wherein the Fcγ receptor-expressing cell is a FcγR⁺ P815 target cell.

5 23. The method of claim 2, wherein the TcR-activating agent is a target antigen bound to an MHC class I molecule on the surface of a target cell, and wherein the first and second T lymphocyte specifically recognize the target antigen.

24. The method of claim 23, wherein the target cell is an EBV-transformed B cell line.

10 25. The method of claim 23, wherein the HSV U_S3-expressing cell and the target cell are the same cell.

26. The method of claim 23, wherein the physiological change is associated with apoptosis of the target cell.

15 27. The method of claim 26, wherein the apoptosis-associated physiological change is lysis of the target cell.

28. The method of claim 27, wherein the target cell is ⁵¹Cr-labeled and lysis of the target cell is determined by detecting release of the ⁵¹Cr from the target cell.

29. The method of claim 26, wherein the apoptosis associated physiological change is activation of a caspase.

20 30. The method of claim 29, wherein the caspase is caspase 3.

31. A method of screening an agent for activity in modulating cytotoxic T lymphocyte (CTL) function, the method comprising:

(1) contacting the agent with

(a) a fibroblast infected with HSV; and/or

25 (b) a CTL;

(2) contacting the HSV-infected fibroblast with the CTL;

(3) contacting a second HSV-infected fibroblast with a second CTL, wherein the second HSV-infected fibroblast and the second CTL are not contacted with the agent;

(4) determining for each of the first and second CTLs the level of a physiological change associated with CTL function; and

5 (5) comparing the relative levels of the physiological change determined for each of the first and second CTLs is to determine whether the agent modulates CTL function.

32. The method of claim 31, wherein the physiological change determined for each of the first and second CTLs is to determine the relative level of phosphorylation of heat shock protein 90 (HSP90) and/or a 50 kD CTL protein, and selecting the agent that
10 reduces or inhibits the relative increase in the level of phosphorylation.

33. The method of claim 32, wherein the fibroblast is infected with HSV-1 or HSV-2.

34. A method for blocking suppression of cytotoxic T cell (CTL) activity against HSV-infected target cells comprising:

15 blocking the expression or functional activity of HSV U_S3.

35. A method for suppressing cytotoxic T cell (CTL) activity against a target antigen in a subject, the method comprising:

isolating a population of antigen presenting cells (APCs) presenting the target antigen on the cell surface;

20 introducing into the APCs an expression vector encoding an HSV U_S3 polypeptide and one or more other HSV proteins, whereby the APCs express the HSV U_S3 polypeptide and one or more other HSV proteins; and

administering to the subject the APCs expressing to the HSV U_S3 polypeptide and one or more other HSV proteins, thereby suppressing CTL activity against the target
25 antigen in the subject.

36. A method of screening an agent for activity in suppressing T lymphocyte function, the method comprising:

(1) contacting the agent with a T lymphocyte;

(2) determining the level of phosphorylation of HSP90 and/or a 50 kD T
30 lymphocyte protein;

(3) comparing the level of phosphorylation of HSP90 and/or the 50 kD T lymphocyte protein in the T lymphocyte contacted with the agent to a T lymphocyte that has not been contacted with the agent; and

(4) selecting the agent that increases the level of phosphorylation of
5 HSP90 and/or 50 kD T lymphocyte protein for suppressing T lymphocyte function.